Complete Summary

GUIDELINE TITLE

Adjuvant therapy for breast cancer.

BIBLIOGRAPHIC SOURCE(S)

Adjuvant therapy for breast cancer. NIH Consens Statement Online 2000 Nov 1-3;17(4):1-23. [2230 references]

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Breast cancer

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Obstetrics and Gynecology
Oncology
Radiology

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Nurses
Patients
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

- To provide clinicians, patients, and the general public with a consensus regarding the use of adjuvant therapy for invasive breast cancer
- To address the following key questions:
    - Which factors should be used to select systemic adjuvant therapy?
    - For which patients should adjuvant hormonal therapy be recommended?
    - For which patients should adjuvant chemotherapy be recommended? Which agents should be used, and at what dose or schedule?
    - For which patients should post-mastectomy radiotherapy be recommended?
    - How do side effects and quality-of-life issues factor into individual decision-making about adjuvant therapy?
    - What are promising new research directions for adjuvant therapy?

TARGET POPULATION

Patients with invasive breast cancer

INTERVENTIONS AND PRACTICES CONSIDERED

1. Hormone therapy (tamoxifen)
2. Chemotherapy
3. Post-mastectomy radiotherapy
4. Decision-making between patients and physicians

MAJOR OUTCOMES CONSIDERED

- Survival (mortality rates)
- Quality of life
- Nodal, menopausal, and hormone receptor status

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The literature was searched through electronic databases including MEDLINE (National Library of Medicine [NLM]), and an extensive bibliography of references was provided to the panel and the conference audience.

The literature search was limited to human subjects research involving treatment, diagnostic testing, and other studies involving adjuvant therapy of breast cancer. Original journal articles, review articles, conference proceedings, meeting abstracts, letters to the editor, and editorials in the English language were included. Publications in languages other than English were excluded. The search time frame included references published primarily between 1995-2000, although a few earlier citations were also selected.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Scientific evidence was given precedence over clinical anecdotal experience.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Consensus Development Conference)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The National Institutes of Health (NIH) Consensus Development Panel on Adjuvant Therapy for Breast Cancer, answering predefined questions, developed their conclusions based on the scientific evidence presented in open forum and the scientific literature. The panel composed a draft statement that was read in its entirety and circulated to the experts and the audience for comment. Thereafter, the panel resolved conflicting recommendations and released a revised statement at the end of the conference.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The National Institutes of Health (NIH) Consensus Development Panel on Adjuvant Therapy for Breast Cancer finalized the revisions within a few weeks after the conference. The draft statement was made available on the World Wide Web immediately following its release at the conference and was updated with the panel's final revisions.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Excerpted by the National Guideline Clearinghouse (NGC):

Generally accepted prognostic and predictive factors include age, tumor size, lymph node status, histological tumor type, grade, mitotic rate, and hormonal receptor status. Novel technologies, such as tissue and expression microarrays and proteomics, hold exciting potential. Progress, however, will depend on proper design and analysis of clinical and pathological investigations.

Decisions regarding adjuvant hormonal therapy should be based on the presence of hormone receptor protein in tumor tissues. Adjuvant hormonal therapy should be offered to women whose tumors express hormone receptor protein. At present, five years of tamoxifen is standard adjuvant hormone therapy; ovarian ablation represents an alternative option for selected premenopausal women. Adjuvant hormonal therapy should not be recommended to women whose tumors do not express hormone receptor protein.

Because adjuvant polychemotherapy improves survival, it should be recommended to the majority of women with localized breast cancer regardless of nodal, menopausal, or hormone receptor status. The inclusion of anthracyclines in adjuvant chemotherapy regimens produces a small but statistically significant improvement in survival over nonanthracycline-containing regimens.

Available data are currently inconclusive regarding the use of taxanes in adjuvant treatment of node-positive breast cancer. The use of adjuvant dose-intensive chemotherapy regimens in high-risk breast cancer and of taxanes in node-negative breast cancer should be restricted to randomized trials. Ongoing studies

evaluating these treatment strategies should be supported to determine if they have a role in adjuvant treatment.

Studies to date have included few patients older than 70 years. There is a critical need for trials to evaluate the role of adjuvant chemotherapy in these women.

There is evidence that women with a high risk of locoregional tumor recurrence after mastectomy benefit from postoperative radiotherapy. This high-risk group includes women with four or more positive lymph nodes or an advanced primary cancer. Currently, the role of post-mastectomy radiotherapy for patients with one to three positive lymph nodes remains uncertain and should be tested in a randomized controlled trial.

Individual patients differ in the importance they place on the risks and benefits of adjuvant treatments. Quality-of-life needs to be evaluated in selected randomized clinical trials to examine the impact of the major acute and long-term side effects of adjuvant treatments, particularly premature menopause, weight gain, mild memory loss, and fatigue. Methods to support shared decision-making between patients and their physicians have been successful in trials; they need to be tailored for diverse populations and should be tested for broader dissemination.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The panel, answering predefined questions, developed their conclusions based on a comprehensive review of scientific evidence presented in open forum. Scientific evidence was given precedence over clinical anecdotal experience.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Adjuvant hormonal therapy

Reductions in the likelihood of tumor recurrence; second primary breast cancer; and death persisting at least 15 years after follow-up.

Chemotherapy

Chemotherapy has been shown to substantially improve the long-term, relapse-free, and overall survival in both premenopausal and postmenopausal women up to age 70 years with node-positive and node-negative disease.

In addition, available data indicate that adjuvant chemotherapy regimens that include an anthracycline result in a small but statistically significant improvement in survival compared to nonanthracycline-containing programs.

Radiotherapy

Randomized controlled trials have demonstrated superior tumor control and overall survival rates with the addition of post-mastectomy radiotherapy.

Decision-making in adjuvant therapy for breast cancer

Findings from current research suggest that decision aids improve patients' knowledge about treatment options, reduce patients' anxiety about treatment decisions and enhance their comfort with treatment choices, and stimulate patients to play a more active role in joint decision-making with their physicians.

Subgroups Most Likely to Benefit:

Hormonal therapy

While the likelihood of benefit from adjuvant hormonal therapy correlates with the amount of hormone receptor protein in tumor cells, patients with any extent of hormone receptor in their tumor cells may still benefit from hormonal therapy.

Chemotherapy

Most women with lymph node metastases or with primary breast cancers larger than 1 cm in diameter (both node-negative and node-positive).

Radiotherapy

Post-mastectomy patients, especially those with a high risk of locoregional tumor recurrence (e.g., women with four or more positive lymph nodes or an advanced primary tumor of 5 centimeters or greater or a tumor invading the skin or adjacent musculature).

POTENTIAL HARMS

Adjuvant Chemotherapy

Studies to date have documented a range of acute and late side effects of adjuvant chemotherapy that have the potential for significantly affecting patients' quality of life. Most acute side effects (e.g., nausea and vomiting, mucositis, hair loss, neutropenia) occur in varying degrees in the different chemotherapy regimens and resolve after treatment completion. This also seems to be true for psychological distress. Several randomized studies have found that the psychological distress patients experience is greater during more toxic adjuvant chemotherapy treatment, resolving soon after treatment completion. Similarly, 1 to 3 years after completing treatment, the distress levels of cancer survivors who had undergone any of the different adjuvant chemoendocrine therapies equal the levels of those who had received no further adjuvant therapy.

The simultaneous combination of chemotherapy plus tamoxifen is associated with an increased risk of thromboembolism when compared to tamoxifen alone. Premature menopause, weight gain, and fatigue are the most frequent long- and short-term problems that have been documented. Several small studies have documented mild cognitive problems, such as those in memory, with precise levels of prevalence and severity yet to be determined. There is also a very small increase in the risk of treatment-related second malignancies and cardiac disease.

Adjuvant Hormone Therapy: Tamoxifen and Ovarian Ablation

Hot flashes and vaginal discharge have been the most common side effects attributed to tamoxifen. Tamoxifen is associated with a small, increased risk of endometrial cancer, pulmonary emboli, and deep vein thrombosis, particularly for women 50 years old or older. The benefits, however, far outweigh the risks. Tamoxifen has not been associated with an increase in depression, weight gain, nausea and vomiting, diarrhea, or problems in sexual functioning.

As with adjuvant chemotherapy, ovarian ablation is associated with the development of premature menopause and its associated symptoms including osteoporosis.

Radiotherapy

Increased risk of arm edema.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This statement is an independent report of the panel and is not a policy statement of the National Institutes of Health (NIH) or the Federal Government.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Adjuvant therapy for breast cancer. NIH Consens Statement Online 2000 Nov 1-3;17(4):1-23. [2230 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2000 Nov 3

GUIDELINE DEVELOPER(S)

National Cancer Institute - Federal Government Agency [U.S.]
National Institutes of Health (NIH) Consensus Development Panel on Adjuvant Therapy for Breast Cancer - Independent Expert Panel

GUIDELINE DEVELOPER COMMENT

National Institutes of Health (NIH) Consensus Statements are prepared by a non-advocate, non-Federal panel of experts, based on (1) presentations by investigators working in areas relevant to the consensus questions during a 2-day public session; (2) questions and statements from conference attendees during open discussion periods that are part of the public session; and (3) closed deliberations by the panel during the remainder of the second day and morning of the third. This statement is an independent report of the panel and is not a policy statement of the National Institutes of Health (NIH) or the Federal Government.

This conference was sponsored by the National Cancer Institute and the National Institutes of Health (NIH) Office of Medical Applications of Research (OMAR). The co-sponsors included the National Institute of Nursing Research and the National Institutes of Health's Office of Research on Women's Health.

SOURCE(S) OF FUNDING

United States Government

GUIDELINE COMMITTEE

National Institutes of Health (NIH) Consensus Development Panel on Adjuvant Therapy for Breast Cancer

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: Patricia Eifel, MD (Panel and Conference Chairperson); John A. Axelson, MD, FACP; Jose Costa, MD; John Crowley, Ph.D.; Walter J. Curran, Jr.,

MD; Ann Deshler, RN; Shirley Fulton, JD, MBA; Carolyn B. Hendricks, MD; Margaret Kemeny, MD; Alice B. Kornblith, PhD; Thomas A. Louis, Ph.D.; Maurie Markman, MD; Robert Mayer, MD; Debra Roter, Dr PH.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All of the panelists who participated in the National Institutes of Health (NIH) conference and contributed to the writing of this consensus statement were identified as having no financial or scientific conflict of interest, and all signed conflict of interest forms attesting to this fact.

ENDORSER(S)

National Institute for Nursing Research - Federal Government Agency [U.S.]
Office of Research on Women's Health (NIH) - Federal Government Agency [U.S.]

GUIDELINE STATUS

This is the current release of the guideline.

An update is not in progress at this time.

GUIDELINE AVAILABILITY

Electronic copies: Available from the NIH Consensus Development Conference Program Web site. Also available from the National Library of Medicine Health Services/Technology Assessment Text (HSTAT) Web site.

Print copies: Available from the NIH Consensus Development Program Information Center, PO Box 2577, Kensington, MD 20891; Toll free phone (in U.S.), 1-888-NIH-CONSENSUS.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- A complete bibliography prepared by the National Library of Medicine (NLM) is available at the NLM Web site.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on May 23, 2001. The information was verified by the guideline developer as of October 25, 2001.

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